For : GELDANAMYCIN AND DERIVATIVES INHIBIT CANCER

INVASION AND IDENTIFY NOVEL TARGETS

Page : 2

In the Claims:

This listing of claims will replace all prior versions and listings of claims in the application:

1. (Currently Amended) A compound of 17-N-Aziridinyl-17-demethoxygeldanamycin Formula 1 or Formula 1

pharmaceutically acceptable salt thereof:

which has the property of inhibiting the activation of Met by HGF/SF in cancer cells at a concentration below 10⁻¹³ M, wherein

R² is a lower alkyl, alkenylor alkynyl; a substituted lower alkyl, alkenyl or alkynyl; a lower alkoy, alkenovy or alkynoxy; a straight or brunched alkylamine; alkenyl amine or alkynyl amine; or a 3-6 member beterocyclic group that is optionally substituted:

R³-is 11, a lower alkyl, alkenyl or alkynyl, a substituted lower alkyl, alkenyl or allynyl; a lower alkony, alkenoxy or alkynyx; a straight or branched alkylamine, alkenyl amine or alkynyl amines; or a 3-6 member heterocyclic group that is optionally substituted:

R² is H: a lower alkyl, alkenyl or alkynyl; a substituted lower alkyl, alkenyl or alkynyl; a lower alkyl, alkenyl or alkynyl; a straight or branched alkylamine, alkenyl amine or alkynyl amine; or wherein the N is a member of a heterocycloalkyl, beterocylokenyl or beterocycloalkyl.

For : GELDANAMYCIN AND DERIVATIVES INHIBIT CANCER

INVASION AND IDENTIFY NOVEL TARGETS

Page : 3

that is optionally substituted;

 R^4 is H; a lower alkyl, alkenyl or alkynyl, a substituted lower alkyl, alkenyl or alkynyl, and wherein

the ring double-bonds between positions $C_0 = C_0$, $C_4 = C_6$, and $C_0 = C_0$ are optionally hydrogenated to single-bonds:

- 2. (Cancelled)
- (Cancelled)
- 4. (Cancelled)
- (Cancelled)
- 6. (Cancelled)
- 7. (Cancelled)
- 8. (Cancelled)
- 9. (Cancelled)
- 10. (Currently Amended) A pharmaceutical compositions comprising
 - (a) the compound of claim 1; and
 - (b) a pharmaceutically acceptable carrier or excipient.
- (Currently Amended) A method of inhibiting a the HGF/SF-induced, Met receptor
 mediated biological activity of a Met-bearing tumor or cancer cell, comprising providing to said

For : GELDANAMYCIN AND DERIVATIVES INHIBIT CANCER

INVASION AND IDENTIFY NOVEL TARGETS

Page : 4

cell[[s]] an effective amount of a compound according to claim 1 of Formula 1 or Formula 11

pharmaceutically acceptable salt thereof;

which compound has an IC_{50} of more than about 10^{30} M for inhibition of said biological activity, wherein

R¹ is a lower alkyl, alkenylor alkynyl; a substituted lower alkyl, alkenyl or alkynyl; a lower alkoxy, alkenoxy or alkynoxy; a straight or branched alkylamine, alkenyl amine or alkynyl amine; or a 3-6 member heterocyclic group that is optionally substituted;

R² is H, a lower alkyl, alkenyl or alkynyl, a substituted lower alkyl, alkenyl or allynyl; a lower alkoxy, alkenoxy or alkynoxy; a straight or branched alkylamine, alkenyl amine or alkynyl amines; or a 3-6 member heterocyclic group that is optionally substituted;

R³ is H; a lower alkyl, alkenyl or alkynyl; a substituted lower alkyl, alkenyl or alkynyl; a lower alkyl, alkenyl or alkynyl; a straight or branched alkylamine, alkenyl amine or alkynyl amine; or wherein the N is a member of a heterocycloalkyl, heterocylokenyl or heteroaryl ring that is optionally substituted;

R⁴ is H; a lower alkyl, alkenyl or alkynyl, a substituted lower alkyl, alkenyl or alkynyl, and wherein

For : GELDANAMYCIN AND DERIVATIVES INHIBIT CANCER

INVASION AND IDENTIFY NOVEL TARGETS

Page : 5

the bonds linking positions C₂ and C₂, C₄ and C₅, and C₈ and C₉ are optionally single bonds.

which commound has an ICs of less than about 10 42 M for inhibition of said biological activity;

- (Original) The method of claim 11 wherein said biological activity is the induction of uPA activity in said cells.
- (Original) The method of claim 11 wherein said biological activity is growth or scatter of said cells.
- 14. (Original) The method of claim 13 wherein said growth of said cells is in vitro.
- 15. (Original) The method of claim 13 wherein said growth of said cells is in vivo.
- (Original) The method of claim 11 wherein said biological activity is invasion of said cells.
- 17. (Original) The method of claim 16 wherein said invasion is in vitro.
- 18. (Original) The method of claim 16 wherein said invasion is in vivo.
- (Original) The method of claim 16 wherein said invasion results in tumor metastasis.
- (Currently Amended) A method of inhibiting in a subject metastasis of Met-bearing tumor or cancer cells that is induced by HGF/SF, comprising providing to said subject an effective amount of a compound according to claim 1 of Formula II

For : GELDANAMYCIN AND DERIVATIVES INHIBIT CANCER

INVASION AND IDENTIFY NOVEL TARGETS

Page : 6

pharmaceutically acceptable salt thereof;

which compound has an IC50 of more than about $10^{-10} M$ of about $10^{-14} M$ -for inhibition of tumor cell invasion when measured in an assay in vitro-.

wherein R¹ is a lower alkyl, alkenylor alkynyl; a substituted lower alkyl, alkenyl or alkynyl; a lower alkoxy, alkenyl amine or alkynyl amine; or a 3-6 member heterocyclic group that is optionally substituted;

R² is H, a lower alkyl, alkenyl or alkynyl, a substituted lower alkyl, alkenyl or allynyl; a lower alkoxy, alkenoxy or alkynoxy; a straight or branched alkylamine, alkenyl amine or alkynyl amines; or a 3-6 member heterocyclic group that is optionally substituted;

R³ is H; a lower alkyl, alkenyl or alkynyl; a substituted lower alkyl, alkenyl or alkynyl; a lower alkoxy, alkenoxy or alkynoxy; a straight or branched alkylamine, alkenyl amine or alkynyl amine; or wherein the N is a member of a heterocycloalkyl, heterocylokenyl or heteroaryl ring that is optionally substituted;

 R^4 is H; a lower alkyl, alkenyl or alkynyl, a substituted lower alkyl, alkenyl or alkynyl, and wherein

the bonds linking positions C₂ and C₃, C₄ and C₅, and C₈ and C₉ are optionally single bonds.

For : GELDANAMYCIN AND DERIVATIVES INHIBIT CANCER

INVASION AND IDENTIFY NOVEL TARGETS

Page : 7

21. (Currently Amended) A method of inhibiting in a subject metastasis of Met-bearing tumor or cancer cells that is induced by HGF/SF, comprising providing to said subject an effective amount of a pharmaceutical composition according to claim 10 which composition comprises a chemical compound that has an IC₅₀ of less-more than about 10⁻¹³M-10⁻¹⁰M for inhibition of tumor cell invasion when measured in an assay in vitro.

- 22. (Previously Presented) The method of claim 11 wherein said inhibition results in measurable regression of a tumor caused by said cells or measurable attenuation of tumor growth in said subject.
- (Currently Amended) A method of protecting against growth or metastasis of a Metpositive tumor in a susceptible subject, comprising administering to said subject who is either
 - (a) at risk for development of said tumor, or
- (b) in the case of an already treated subject, at risk for recurrence of said tumor, an effective amount of the compound of elaim 1 a compound of Formula II or Formula II

For : GELDANAMYCIN AND DERIVATIVES INHIBIT CANCER

INVASION AND IDENTIFY NOVEL TARGETS

Page: 8

which compound has an IC₂₀ of more than about 10⁻¹⁰M for inhibiting. Met activation of uPA in cancer cells,

wherein R¹ is a lower alkyl, alkenylor alkynyl; a substituted lower alkyl, alkenyl or alkynyl; a lower alkoxy, alkenyx or alkynyl; a straight or branched alkylamine, alkenyl amine or alkynyl amine; or a 3-6 member heterocyclic group that is optionally substituted;

R² is H, a lower alkyl, alkenyl or alkynyl, a substituted lower alkyl, alkenyl or alkynyl; a lower alkoxy, alkenoxy or alkynoxy; a straight or branched alkylamine, alkenyl amine or alkynyl amines; or a 3-6 member heterocyclic group that is optionally substituted;

R³ is H; a lower alkyl, alkenyl or alkynyl; a substituted lower alkyl, alkenyl or alkynyl; a lower alkoxy, alkenoxy or alkynoxy; a straight or branched alkylamine, alkenyl amine or alkynyl amine; or wherein the N is a member of a heterocycloalkyl, heterocylokenyl or heteroaryl ring that is optionally substituted;

R² is H; a lower alkyl, alkenyl or alkynyl, a substituted lower alkyl, alkenyl or alkynyl, and wherein

the bonds linking positions C_2 and C_3 , C_4 and C_5 , and C_8 and C_9 are optionally single bonds.

- 24. (Original) The method of claim 23 wherein the subject is a human.
- 25. (Currently Amended) A method of inducing an antitumor or anticancer response in a mammal having an HGF-responsive Met-expressing tumor, comprising administering to said mammal an effective amount of the compound of claim 1 to said mammal, a compound of Formula I or Formula II

For : GELDANAMYCIN AND DERIVATIVES INHIBIT CANCER

INVASION AND IDENTIFY NOVEL TARGETS

Page : 9

pharmaceutically acceptable salt thereof, at a concentration of more than about 10-19M;

wherein R¹ is a lower alkyl, alkenylor alkynyl; a substituted lower alkyl, alkenyl or alkynyl; a lower alkoxy, alkenoxy or alkynoxy; a straight or branched alkylamine, alkenyl amine or alkynyl amine; or a 3-6 member heterocyclic group that is optionally substituted;

R⁷ is H, a lower alkyl, alkenyl or alkynyl, a substituted lower alkyl, alkenyl or allynyl, a lower alkony, alkenony or alkynoxy; a straight or branched alkylamine, alkenyl amine or alkynyl amines; or a 3-6 member heterocyclic group that is optionally substituted;

R³ is H; a lower alkyl, alkenyl or alkynyl; a substituted lower alkyl, alkenyl or alkynyl; a lower alkoxy, alkenoxy or alkynoxy; a straight or branched alkylamine, alkenyl amine or alkynyl amine; or wherein the N is a member of a heterocycloalkyl, heterocylokenyl or heteroaryl ring that is optionally substituted;

R⁴ is H; a lower alkyl, alkenyl or alkynyl, a substituted lower alkyl, alkenyl or alkynyl, and wherein

the bonds linking positions C_2 and C_3 , C_4 and C_5 , and C_6 and C_9 are optionally single bonds.

thereby inducing an antitumor or anticancer response which is

(a) a partial response characterized by

For : GELDANAMYCIN AND DERIVATIVES INHIBIT CANCER

INVASION AND IDENTIFY NOVEL TARGETS

Page : 10

 at least a 50% decrease in the sum of the products of maximal perpendicular diameters of all measurable lesions;

- (ii) no evidence of new lesions, and
- (iii) no progression of any preexisting lesions, or
- (b) a complete response characterized by the disappearance of all evidence of tumor or cancer disease for at least one month.
- (Original) The method of claim 25 wherein said antitumor or anticancer response is a
 partial antitumor or anticancer response.
- 27. (Previously Presented) The method of claim 25 wherein the mammal is a human.
- (Previously Presented) A compound according to claim 1 which is detectably labeled with a halogen radionuclide.
- 29. (Original) The compound of claim 28 wherein the radionuclide is bonded to the R¹ group.
- 30. (Previously Presented) The compound of claim 28 wherein the radionuclide is selected from the group consisting of 18 F, 76 Br, 123 I, 124 I, and 131 I.
- 31. (Previously Presented) A method of imaging a tumor in a subject comprising administering an effective amount of a labeled compound according to claim 28, and imaging the detectable label with an imaging means.
- 32. (New) The method of claim 11 wherein the compound is a benzoquinone of Formula I.
- 33. (New) The method of claim 11 wherein the compound is a hydroquinone of Formula II.

For : GELDANAMYCIN AND DERIVATIVES INHIBIT CANCER

INVASION AND IDENTIFY NOVEL TARGETS

Page : 1

- 34. (New) The method of claim 11 wherein R¹ is a 3-6 member heterocyclic ring in which the heteroatom is N.
- 35. (New) The method of claim 11 wherein each of R², R³ and R⁴ of the compound is H.
- 36. (New) The method of claim 11 wherein the compound is selected from the group consisting of:
 - (a) 17-(2-Fluoroethyl)amino-17-demethoxygeldanamycin;
 - (b) 17-Allylamino-17-demethoxygeldanamycin;
 - (c) 17-N-Aziridinyl-17-demethoxygeldanamycin;
 - (d) 17-Amino-17-demethoxygeldanamycin;
 - (e) 17-N-Azetidinyl-17-demethoxygeldanamycin;
 - (f) 17-(2-Dimethylaminoethyl)amino-17-demethoxygeldanamycin;
 - (g) 17-(2-Chloroethyl)amino-17-demethoxygeldanamycin; and
 - (h) Dihydrogeldanamycin.